Response to Comment on: Keenan et al. (2010) Residual Insulin Production and Pancreatic ß-Cell Turnover After 50 Years of Diabetes: Joslin Medalist Study. Diabetes 2010;59:2846–2853

Response to Comment on: Keenan et al. (2010) Residual Insulin Production and Pancreatic β-Cell Turnover After 50 Years of Diabetes: Joslin Medalist Study. Diabetes 2010;59:2846–2853

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We appreciate the response by Rother and Harlan (1) to our article (2). However, it is difficult to understand what the confirmatory aspects of the Medalist Study data are with respect to the studies of Liu et al. (3) and Rother et al. (4), which documented minimal levels of C-peptide production in individuals with a diabetes duration of 19.2 ± 11.8 years and 21.3 ± 10.7 years, respectively. Clearly, this duration is significantly lower than the Medalists' mean duration of 56.2 ± 5.8 years. Another difference is the relationship of disease duration and residual C-peptide production, which was not significant in the Medalist Study but was reported to be significant in the article by Liu et al., with a statistically higher mean duration ($P = 0.0045$) in those patients without (26.2 ± 13.1 years) than those patients with residual C-peptide production (19.2 ± 11.8 years) (3).

One of the most important components of our study is the pre- and post mortem data on nine Medalists. Ours is the first study to show a correlation between random C-peptide, physiological response to stimulation, and insulin positive β-cell mass in any human population of type 1 diabetic patients and, extraordinarily, in individuals with a mean of 55 years of diabetes. Although this part of the study included only nine patients, each had insulin positive cells even after their extreme duration of diabetes.

Although our findings of stimulated C-peptide may be an underestimation of islet secretory capacity as suggested by Rother and Harlan, because of exogenous insulin injection before the mixed-meal tolerance test, only 6 of the 31 subjects took insulin the morning of the test, and that was to bring their fasting blood glucose values to under 250 mg/dl, a safe range for the test to be performed. We hope these explanations have provided a clear differentiation between our Medalist Study and previous publications.

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